Chapter XVI-4

PULMONARY FUNCTION AND DISEASE

Bronchitis, cough, dyspnea and acute respiratory irritation and distress have been reported as acute effects following exposure to phenoxy herbicides and dioxin (Berwick, 1970; Bauer et al, 1961; Bashirov, 1969). Little is known about the presence or absence of chronic pulmonary disease following herbicide exposure. These acute effects and the high likelihood of inhalation exposure to herbicide among operation Ranch Hand personnel in Vietnam prompted the evaluation of the pulmonary status of the study participants. In-home questionnaire responses concerning history of pulmonary disease were reviewed to determine the history of reported pulmonary disease in the Ranch Hand and comparison groups. The analysis of past pulmonary disease included data from the total comparison group. All other analyses in this subchapter were performed on all Ranch Hand individuals (1045) and the subset of original comparisons (773) who participated in the physical examination, except for a few individuals omitted due to missing pulmonary function data. Table XVI-4-1 presents the distribution of reported pulmonary disease in the Ranch Hand group, the entire comparison group, and in the subset of original comparisons.

Table XVI-4-1

DISTRIBUTION OF REPORTED PULMONARY DISEASE IN THE RANCH HAND AND COMPARISON GROUPS

	Group		
Diagnosis (ICD-9 Code)	Original Comparison	Ranch Hand	Total Comparison
Tuberculosis and fungal infection (010-018; 114-116)	9	11	10
Pneumonia and Acute infections (480-487; 460-466)	10	6	11
Neoplasia (160-165; 212)	1	3	2
Chronic sinusitis and other upper respiratory disease (470-478; 480-519)	426	689	687
	P=0.20	P=0.63	

The distribution of reported disease is not significantly different between the Ranch Hand group and either the original comparisons or the entire comparison group.

Two measures of pulmonary function obtained during the physical examination and a third variable, derived from the other two, were analyzed. The forced expiratory volume in one second (FEV_1) and the forced vital capacity (FVC) were determined. Prior to being analyzed, these two quantities were expressed as a percent of the predicted values for healthy, nonsmoking males (Morris et al, 1971). The third variable analyzed was the derived ratio of FEV_1 to FVC. Group differences were tested using both an unadjusted one-way analysis of variance and an analysis of covariance adjusting for age and smoking habits. The results of the analysis of the unadjusted mean values for the FVC, FEV_1 and the FEV_1/FVC ratio are presented in Table XVI-4-2.

Table XVI-4-2

ANALYSIS OF THE UNADJUSTED MEANS OF PULMONARY FUNCTION PARAMETER

Parameter	Group	N	Mean	Std. Dev.	P Value
FVC (%Predicted)	Ranch Hand	1033	98.87%	13.15	0.97
	Comparison	761	98.84%	12.98	
FEV_1 (% Predicted)	Ranch Hand	1033	105.58%	15.65	0.69
	Comparison	761	105.87%	15.36	
FEV_1/FVC	Ranch Hand	1035	0.8031%	0.0663	0.87
	Comparison	764	0.8026%	0.0670	

There are no significant unadjusted group differences between the Ranch Hand and comparison group. However, there were statistically significant interactions between age, group and pulmonary function in the analysis of both FVC and FEV_1 ($P = 0.04$ and 0.01 respectively). Similarly, smoking habits interacted significantly with the FEV/FVC ratio ($P = 0.03$). As a result, fully adjusted testing was considered to be inappropriate. However, comparison of the regression planes using the mean values of the covariables revealed P values of 0.86, 0.79, and 0.85 respectively for the FVC, FEV_1 and FEV_1/FVC ratio. These values are observed to be quite similar to those seen in the unadjusted analyses.

An analysis of variance of the unadjusted means for low, medium, and high exposure among the Ranch Hand group was conducted in each occupational category. These analyses revealed no consistent association between exposure level and pulmonary function. The results are presented in Table XVI-4-3. The only significant findings were in the FEV_1/FVC ratio in the enlisted categories. However, these findings were inconsistent, with the lowest exposed individuals in the enlisted flying category having the lowest mean ratio (percent performance) and higher exposed individuals doing better. In the enlisted ground personnel the mean ratio was lowest in the most heavily exposed group. Thus, while statistically significant, these findings do not conform to classic dose-response relationships.

Table XVI-4-3

HERBICIDE EXPOSURE ANALYSIS OF PULMONARY FUNCTION PARAMETERS, UNADJUSTED FOR COVARIATES OF AGE AND SMOKING

Occupational Category	Parameter	Exposure Level	N	Mean	Std Dev	P Value
Officer	FVC (% Predicted)	Low	110	100.81	12.80	0.55
		Medium	128	99.61	13.53	
		High	125	101.40	12.96	
	FEV_1 (% Predicted)	Low	110	108.17	15.46	0.69
		Medium	128	107.27	16.37	
		High	125	108.94	14.46	
	FEV_1/FVC	Low	110	0.799	0.067	0.64
		Medium	128	0.792	0.062	
		High	125	0.798	0.056	
Enlisted Flying	FVC	Low	56	99.84	14.19	0.24
		Medium	57	95.78	11.88	
		High	65	96.68	14.12	
	FEV_1	Low	56	102.75	17.36	0.90
		Medium	57	104.13	14.52	
		High	65	103.80	16.89	
	FEV_1/FVC	Low	56	0.768	0.070	0.003
		Medium	58	0.819	0.106	
		High	65	0.803	0.063	
Enlisted Ground	FVC	Low	150	98.22	12.17	0.87
		Medium	178	98.44	13.88	
		High	145	97.70	11.97	
	FEV_1	Low	150	105.60	14.54	0.16
		Medium	178	105.00	15.42	
		High	145	102.47	14.85	
	FEV_1/FVC	Low	150	0.817	0.056	0.0005
		Medium	178	0.819	0.058	
		High	146	0.794	0.068	

Analyses of covariance adjusting for age and smoking were possible in some of the occupational categories, and the results of these analyses are presented in Table XVI-4-4.

Table XVI-4-4

ANALYSES OF PULMONARY FUNCTION AND HERBICIDE EXPOSURE, ADJUSTED FOR SMOKING AND AGE

Occupational Category	Parameter	P Value for the Exposure Analysis
Officer	FVC	0.26
	FEV_1	0.28
	FEV_1/FVC	0.68
Enlisted Flying	FVC	0.13*
	FEV_1	0.90*
	FEV_1/FVC	0.004
Enlisted Ground	FVC	0.62
	FEV_1	0.47
	FEV_1/FVC	0.03*

*= Significant covariable interaction

These adjusted analyses identified significant associations in the FEV_1/FVC ratio in both enlisted categories. However, there was significant interaction between exposure level, the FEV_1/FVC ratio, smoking habits and age in the enlisted ground category. As noted in Table XVI-4-4, there was also interaction in the enlisted flying category for both FVC and FEV_1. When the regression planes were compared using the mean values of the age and smoking covariables, the resultant P values were as follows: Enlisted flying, FVC P = 0.10; Enlisted flying FEV_1 P = 0.98; Enlisted ground FEV_1/FVC P = 0.02. These P values are essentially the same as those observed in the interactions. They are also similar to those seen in the unadjusted analyses. As noted in the unadjusted analysis in Table XVI-4-3 the pattern did not suggest a consistent dose response.

Summary

In a few instances the results of the statistical analyses revealed significant ($P \leq 0.05$) or suggestive ($P = 0.10$ to 0.20) differences in pulmonary function. There were no differences detected between the Ranch Hand and comparison groups. Where significant differences were noted in the exposure index analyses, they were isolated and inconsistent in character. There were differences in the age by smoking by exposure interaction in the two groups, but it is not possible to characterize these further at this time. It may be possible to clarify these differences during follow-up phases of the study. In summary, there is no indication in the baseline physical examination that exposure to herbicide in Vietnam adversely affected pulmonary function as measured 10 to 20 years after the exposure.